

Claims:

1. A method of screening for a compound that regulates the activity of a cell surface protein, the method comprising determining the activity or cellular location of tropomyosin in the presence of a candidate compound, wherein altered tropomyosin activity or cellular location in the presence of the compound when compared to the absence of the compound indicates that the compound regulates the activity of a cell surface protein.
2. A method according to claim 1 wherein altered cellular location of tropomyosin in the presence of the compound indicates that the compound increases the activity of a cell surface protein.
3. A method of screening for a compound that regulates the activity of a cell surface protein, the method comprising determining the expression levels of tropomyosin in the presence of a candidate compound, wherein altered tropomyosin expression in the presence of the compound when compared to the absence of the compound indicates that the compound regulates the activity of a cell surface protein.
4. A method according to claim 3 wherein reduced tropomyosin expression in the presence of the compound indicates that the compound increases the activity of a cell surface protein.
5. A method of screening for a compound that regulates the activity of a cell surface protein, the method comprising measuring the binding of tropomyosin to one of its binding partners in the presence of a candidate compound, wherein an altered level of binding of tropomyosin to its binding partner in the presence of the compound when compared to the absence of the compound indicates that the compound regulates the activity of a cell surface protein.
6. A method according to claim 5 wherein a reduced level of binding of tropomyosin to its binding partner in the presence of the compound indicates that the compound increases the activity of a cell surface protein.

7 A method according to claim 5 or claim 6 wherein the tropomyosin binding partner is selected from the group consisting of calponin, CEACAM1, endostatin, Enigma, Gelsolin (preferably sub-domain 2), S100A2 and actin.

5 8. A method according to claim 7 wherein the tropomyosin binding partner is actin.

9. A method according to any one of claims 1 to 8 wherein the cell surface protein is selected from the group consisting of a transport protein, a channel, a receptor, a
10 growth factor, an antigen, a signalling protein and a cell adhesion protein.

10. A method according to claim 9 wherein the protein is a transport protein or a channel.

15 11. A method of screening for a therapeutic compound for the treatment of cystic fibrosis, the method comprising determining the activity or cellular location of tropomyosin in the presence of a candidate compound, wherein altered tropomyosin activity or cellular location in the presence of the compound when compared to the absence of the compound indicates that the compound is useful for the treatment of
20 cystic fibrosis.

12. A method according to claim 11 wherein altered cellular location of tropomyosin in the presence of the compound indicates that the compound is useful for the treatment of cystic fibrosis.

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13. A method of screening for a therapeutic compound for the treatment of cystic fibrosis, the method comprising determining the expression levels of tropomyosin in the presence of a candidate compound, wherein altered tropomyosin expression in the presence of the compound when compared to the absence of the compound indicates
30 that the compound is useful for the treatment of cystic fibrosis.

14. A method according to claim 13 wherein reduced tropomyosin expression in the presence of the compound indicates that the compound is useful for the treatment of cystic fibrosis.

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15. A method of screening for a therapeutic compound for the treatment of cystic fibrosis, the method comprising measuring the binding of tropomyosin to one of its binding partners in the presence of a candidate compound, wherein an altered level of binding of tropomyosin to its binding partner in the presence of the compound when
5 compared to the absence of the compound indicates that the compound is useful for the treatment of cystic fibrosis.

16. A method according to claim 15 wherein a reduced level of binding of tropomyosin to its binding partner in the presence of the compound indicates that the
10 compound is useful for the treatment of cystic fibrosis.

17. A method according to claim 15 or claim 16 wherein the tropomyosin binding partner is selected from the group consisting of calponin, CEACAM1, endostatin, Enigma, Gelsolin (preferably sub-domain 2), S100A2 and actin.
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18. A method according to claim 17 wherein the tropomyosin binding partner is actin.

19. A method according to any one of claims 1 to 18 wherein the method further
20 comprises formulating the identified compound for administration to a human or a non-human animal.

20. A method for regulating the insertion or retention of a protein in a cell surface membrane, the method comprising administering to the cell an agent that modulates
25 tropomyosin expression, location or activity.

21. A method according to claim 20 wherein the insertion or retention of the protein in the cell surface membrane is increased by administering a tropomyosin antagonist to the cell.
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22. A method according to claim 20 or claim 21 wherein the protein is selected from the group consisting of a transport protein, a channel, a receptor, a growth factor, an antigen, a signalling protein and a cell adhesion protein.

23. A method according to claim 22 wherein the transport protein is the cystic fibrosis transmembrane conductance regulator (CFTR).
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24. A method for regulating the transport of molecules into or out of a cell, the method comprising administering to the cell an agent that modulates tropomyosin expression, location or activity.
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25. A method according to claim 24 wherein the transport of molecules into or out of the cell is increased by administering a tropomyosin antagonist to the cell.
26. A method according to claim 24 or claim 25 wherein the molecules are selected
- 10 from the group consisting of electrolytes, water, monosaccharides and ions.
27. A method for the treatment or prevention of a disease in a subject caused by the abnormal insertion, retention or activity of a cell surface membrane protein, the method comprising administering to the subject an agent that modulates tropomyosin
- 15 expression, location or activity.
28. A method according to any one of claims 20 to 27 wherein the cell is a non-muscle cell.
- 20 29. A method according to claim 28 wherein the cell is a neuronal cell or an epithelial cell.
30. A method according to claim 29 wherein the epithelial cell is a gastrointestinal epithelial cell.
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31. A method according to claim 27 wherein the disease caused by the abnormal insertion or activity of a cell surface membrane protein is selected from the group consisting of cystic fibrosis, multiple sclerosis, polycystic kidney disease, viral infection, bacterial infection, reperfusion injury, Menkes Disease, Wilson's Disease,
- 30 diabetes, myotonic dystrophies, epilepsy and mood disorders such as depression, bipolar disorder or dysthymic disorder.
32. A method for the treatment or prevention of a cystic fibrosis in a subject, the method comprising administering to the subject an agent that modulates tropomyosin
- 35 expression, location or activity.

33. A method according to any one of claims 1 to 32 wherein the tropomyosin is an isoform encoded by a gene selected from the group consisting of TPM 1, TPM 2, TPM 3 and TPM 4.
- 5 34. A method according to claim 33 wherein the tropomyosin isoform is selected from the group consisting of TM1, TM2, TM3, TM4, TM5, TM5a, TM5b, TM6, Tm5NM-1, Tm5NM-2, Tm5NM-3, Tm5NM-4, Tm5NM-5, Tm5NM-6, Tm5NM-7, Tm5NM-8, Tm5NM-9, Tm5NM-10, and Tm5NM-11.
- 10 35. A method according to claim 34 wherein the tropomyosin isoform comprises an amino acid sequence encoded by exon 1b of the TPM 1 gene (SEQ ID NO:11) or an amino acid sequence encoded by exon 1b of the TPM 3 gene (SEQ ID NO:12).
- 15 36. A method according to claim 34 wherein the tropomyosin isoform is TM5a or TM5b.
37. A method according to any one of claims 20 to 36 wherein the agent is a tropomyosin antagonist selected from the group consisting of a peptide, an antibody directed against tropomyosin, a small organic molecule, an antisense compound
20 directed against tropomyosin-encoding mRNA, an anti-tropomyosin catalytic molecule such as a ribozyme or a DNAzyme, and a dsRNA or small interfering RNA (RNAi) molecule that targets tropomyosin expression.
38. A method according to claim 37 wherein the tropomyosin antagonist is an
25 antisense compound, a catalytic molecule or an RNAi molecule directed against tropomyosin-encoding mRNA.
39. A method according to claim 37 wherein the tropomyosin antagonist is an antisense compound, a catalytic molecule or an RNAi molecule targeted specifically
30 against exon 1b of the TPM 1 gene (SEQ ID NO:7) or exon 1b of the TPM 3 gene (SEQ ID NO:8).
40. A method according to claim 37 wherein the tropomyosin antagonist is an antisense compound, a catalytic molecule or an RNAi molecule targeted to the
35 sequence AGCTCGCTGGAGGCGGTG (SEQ ID NO:13).

41. A method according to claim 37 wherein the tropomyosin antagonist is an antisense compound comprising the sequence CACCGCCUCCAGCGAGCT (SEQ ID NO:14).

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42. A method for assessing an individual's predisposition to a disease caused by the abnormal insertion, retention or activity of a cell surface membrane protein, the method comprising the step of determining the presence of a mutation in a tropomyosin gene of the individual.

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43. A method for assessing an individual's predisposition to a disease caused by the abnormal insertion, retention or activity of a cell surface membrane protein, the method comprising analysing the polarised distribution of tropomyosin in the cells of the individual.